L Number	Hits	Search Text	DB	Time stamp
1	9	GUNZBURG NEAR Walter	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/05 10:06
4	3617	cytochrome ADJ p450	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/05 10:16
5	351911	encapsula$6 capsul$6 microencapsul$6	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/02/05 10:10
6	1	(cytochrome ADJ p450) NEAR (encapsula$6 capsul$6 microencapsul$6)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/02/05 10:10
7	61	(cytochrome ADJ p450) SAME (encapsula$6 capsul$6 microencapsul$6)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/02/05 10:16
8	253	cytochrome ADJ p450.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/05 10:16
9	2	(cytochrome ADJ p450.clm.) SAME (encapsula$6 capsul$6 microencapsul$6)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/02/05 10:16
10	17	(US-5688773-$ or US-6207648-$ or US-6540995-$ or US-6048551-$ or US-5759765-$ or US-6117681-$ or US-6656727-$ or US-5605835-$ or US-5981211-$).did. or (US-20010043921-$ or US-20020061297-$ or US-20020085998-$ or US-20020085995-$ or US-20020082224-$ or US-20020064872-$).did. or (WO-9735994-$ or WO-200262969-$).did.	USPAT; US-PGPUB; DERWENT	2004/02/05 10:17

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(FILE 'HOME' ENTERED AT 10:17:26 ON 05 FEB 2004)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 10:17:36 ON 05 FEB 2004

L1 55568 S CYTOCHROME P450
L2 289103 S ENCAPSULA? OR CAPSUL? OR MICROENCAPSUL? OR MICROSPHERE?
L3 149 S L1 (L) L2
L4 90 DUP REM L3 (59 DUPLICATES REMOVED)
L5 31 S L4 AND PY<=1997
L6 31 FOCUS L5 1-
L7 54 S L4 AND CELL?
L8 54 FOCUS L7 1-

=> d an ti so au ab l8 1 2 6 7 8

L8 ANSWER 1 OF 54 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:412996 CAPLUS
DN 129:140515
TI **Encapsulated cells** engineered to produce an ifosfamide activating **cytochrome P450** in the vicinity of pancreatic tumors for targeted chemotherapy
SO Nucleic Acids Symposium Series (1998), 38(Advances in Gene Technology: Molecular Biology in the Conquest of Disease), 171-172
CODEN: NACSD8; ISSN: 0261-3166
AU Gunzburg, Walter H.; Karle, Peter; Muller, Petra; Jesnowski, Ralf; Nizze, Horst; Liebe, Stefan; Salmons, Brian; Lohr, Matthias
AB A system is developed for the local conversion of ifosfamide to the toxic forms at the site of pancreatic adenocarcinoma. **Cells** expressing cytochrome P 450 2B1 were encapsulated in **cellulose** sulfate and implanted in nude mice with human pancreatic adenocarcinoma, following the systemic treatment with ifosfamide. Of the 22 mice treated, 12 showed a redn. in tumor mass of >50%, and in 4 of these mice the tumor was no longer detectable. This therapeutic effect was due to the encapsulated **cells** since only .apprx.30% of the mice receiving ifosfamide alone (or non-encapsulated **cells** and ifosfamide) showed a benefit. In addn., the degree of necrosis was much higher in those mice receiving the encapsulated **cells** and ifosfamide.

L8 ANSWER 2 OF 54 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:546443 CAPLUS
DN 138:78227
TI Microencapsulation of genetically engineered **cells** for cancer therapy
SO Methods in Enzymology (2002), 346(Gene Therapy Methods), 603-618
CODEN: MENZAU; ISSN: 0076-6879
AU Loehr, J.-Matthias; Saller, Robert; Salmons, Brian; Guenzburg, Walter H.
AB The use of genetically engineered, microencapsulated **cells** in cancer therapy using pancreatic carcinoma as a model system is described. Thus, transgenic **cells** expressing the rat CYP2B1 gene are encapsulated using sodium **cellulose** sulfate and poly(diallyldimethylammonium chloride). The encoding cytochrome P 450 converts ifosfamide into phohsphoramide and acrolein. (c) 2002 Academic Press.

L8 ANSWER 6 OF 54 MEDLINE on STN
AN 1999150919 MEDLINE
TI Intratumoral injection of **encapsulated cells** producing an oxazaphosphorine activating **cytochrome P450** for targeted chemotherapy.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1998) 451 97-106.
Journal code: 0121103. ISSN: 0065-2598.
AU Karle P; Muller P; Renz R; Jesnowski R; Saller R; von Rombs K; Nizze H; Liebe S; Gunzburg W H; Salmons B; Lohr M
AB The prognosis of pancreatic adenocarcinoma is poor and current treatment is for the most part ineffective. We describe here a novel treatment strategy using a mouse model system for pancreatic cancer. Human embryonic epithelial **cells** have been genetically modified to

express the **cytochrome P450** 2B1 enzyme under the control of a CMV immediate-early promoter. This CYP2B1 gene converts oxazaphosphorines (ifosfamide or cyclophosphamide) to their active cytotoxic compounds, phosphoramide mustard, which alkylates DNA, and acrolein, which alkylates proteins. A number of assays were performed to demonstrate the CYP2B1 gene function as well as toxic effects on neighbouring **cells** (bystander effect). The **cells** were then **encapsulated** in a **cellulose** sulphate formulation shown to be well tolerated in the pancreas of immunocompetent mice, and injected 1 cm away from pre-established tumours derived from a human pancreatic tumour **cell** line (PaCa-44). Intraperitoneal administration of low-dose ifosfamide to tumour bearing mice that received the **encapsulated cells** results in partial or even complete tumour ablation. Such an in situ chemotherapy strategy utilizing genetically modified **cells** in an immunoprotected environment may prove useful for solid tumour therapy in man.

L8 ANSWER 7 OF 54 MEDLINE on STN
AN 1999344367 MEDLINE
TI Injection of **encapsulated cells** producing an ifosfamide-activating **cytochrome P450** for targeted chemotherapy to pancreatic tumors.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999 Jun 30) 880 337-51. Journal code: 7506858. ISSN: 0077-8923.
AU Muller P; Jesnowski R; Karle P; Renz R; Saller R; Stein H; Puschel K; von Rombs K; Nizze H; Liebe S; Wagner T; Gunzburg W H; Salmons B; Lohr M
AB The prognosis of pancreatic cancer is poor, and current medical treatment is mostly ineffective. The aim of this study was to design a new treatment modality in an animal model system. We describe here a novel treatment strategy employing a mouse model system for pancreatic carcinoma. Embryonal kidney epithelial **cells** were genetically modified to express the **cytochrome P450** subenzyme 2B1 under the control of a cytomegalovirus (CMV) immediate early promoter. This CYP2B1 gene converts ifosfamide to its active cytotoxic compounds, phosphoramide mustard, which alkylates DNA, and acrolein, which alkylates proteins. The **cells** were then **encapsulated** in a **cellulose** sulphate formulation and implanted into preestablished tumors derived from a human pancreatic tumor **cell** line. Intraperitoneal administration of low-dose ifosfamide to tumor bearing mice that received the **encapsulated cells** results in partial or even complete tumor ablation. Such an in situ chemotherapy strategy utilizing genetically modified **cells** in an immunoprotected environment may prove useful for solid tumor therapy in man.

L8 ANSWER 8 OF 54 MEDLINE on STN
AN 1999257880 MEDLINE
TI Targeted chemotherapy by intratumour injection of **encapsulated cells** engineered to produce CYP2B1, an ifosfamide activating **cytochrome P450**.
SO GENE THERAPY, (1998 Aug) 5 (8) 1070-8. Journal code: 9421525. ISSN: 0969-7128.
AU Lohr M; Muller P; Karle P; Stange J; Mitzner S; Jesnowski R; Nizze H; Nebe B; Liebe S; Salmons B; Gunzburg W H
AB The prognosis of pancreatic adenocarcinoma is poor and current treatment ineffective. A novel treatment strategy is described here using a mouse model system for pancreatic cancer. **Cells** that have been genetically modified to express the **cytochrome P450** 2B1 enzyme are **encapsulated** in **cellulose** sulphate and implanted into pre-established tumours derived from human pancreatic **cells**. **Cytochrome P450** 2B1 converts the chemotherapeutic agent ifosfamide to toxic metabolites. Administration of ifosfamide to tumour-bearing mice that were recipients of implanted **encapsulated cells** results in partial or even complete tumour ablation. These results suggest that in situ chemotherapy with genetically modified **cells** in an immunoprotected environment may prove useful for application in man.

SEARCH HISTORY